



# Estimating the Effect of Depression on HIV Transmission Risk Behaviors Among People Who Inject Drugs in Vietnam: A Causal Approach

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## Abstract

The burden of depression and HIV is high among people who inject drugs (PWID), yet the effect of depression on transmission risk behaviors is not well understood in this population. Using causal inference methods, we analyzed data from 455 PWID living with HIV in Vietnam 2009–2013. Study visits every 6 months over 2 years measured depressive symptoms in the past week and injecting and sexual behaviors in the prior 3 months. Severe depressive symptoms (vs. mild/no symptoms) increased injection equipment sharing (risk difference [RD] = 3.9 percentage points, 95% CI –1.7, 9.6) but not condomless sex (RD = –1.8, 95% CI –6.4, 2.8) as reported 6 months later. The cross-sectional association with injection equipment sharing at the same visit (RD = 6.2, 95% CI 1.4, 11.0) was stronger than the longitudinal effect. Interventions on depression among PWID may decrease sharing of injection equipment and the corresponding risk of HIV transmission.

**Clinical trial registration** ClinicalTrials.gov NCT01689545.

**Keywords** People who inject drugs · HIV transmission · Depressive symptoms · Sexual behavior · Injecting behavior · Marginal structural models

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## Introduction

Despite global progress in combating the HIV epidemic, people who inject drugs (PWID) remain disproportionately at risk of HIV infection in southeast and central Asia and eastern Europe [1–5]. Sharing injection equipment is one of the most efficient means of HIV transmission [6, 7], and in these regions, PWID have limited access to and suboptimal use of harm reduction services and antiretroviral therapy (ART) [8, 9]. The persistence of injection drug use and viremia, without adequate preventive services, results in a high risk of HIV transmission to injecting or sexual partners [10].

The burden of depression is high among PWID and may further interfere with HIV prevention efforts. Up to 50% of PWID suffer from severe depressive symptoms [11–15], and the presence and severity of depressive symptoms are closely linked to frequency of injection and risk of relapse, suggesting a bidirectional relationship between depression and injection drug use [16–18]. Comorbid depression consistently results in poor HIV treatment outcomes, such as lowering ART use and viral suppression [19–24].

Depression may be an important driver of continued HIV transmission among PWID if symptoms increase transmission risk behaviors (e.g., sharing injection drug use equipment, engaging in condomless sex) in the absence of viral suppression. However, while the deleterious effect of depression on HIV treatment outcomes is well established across populations, its effect on the injecting and sexual behaviors that can facilitate HIV transmission or acquisition is not well understood among PWID. Although there is substantial evidence that depression increases sexual risk behaviors among men who have sex with men (MSM) [25–29], few studies have focused on PWID and assessed injecting behaviors. Specifically, in Vietnam, the focus of this study and a setting where the HIV epidemic is concentrated among men who inject drugs [30, 31], there have been no prior studies of the relationship of depression with injecting and sexual behaviors.

Existing studies on depression and HIV transmission risk behaviors among PWID have suffered from several methodological limitations. To our knowledge, all previous studies that include PWID populations have assessed only correlations between depression and transmission risk behaviors, without inferring causality [32–40]. In these studies, depression and risk behaviors have typically been evaluated for the same time period (e.g., self-report covering the last month), without the ability to infer whether depression preceded risk behaviors or vice versa [35–37, 39, 40]. Potential confounders of the relationship between depression and risk behaviors were also measured for the same retrospectively assessed time period. Studies that used traditional statistical adjustment for these contemporaneous covariates [34, 38] may have induced bias if these variables acted as causal mediators rather than confounders [41]. In addition, although depression is known to be episodic [42], prior analyses have primarily relied on a single assessment rather than accounting for changes in both depressive symptoms and time-varying confounders [33, 34, 38, 40].

Possibly stemming from these methodological issues, existing evidence for an association between depression and transmission risk behaviors in PWID is inconsistent. While an early meta-analysis (that included studies among PWID) found little evidence for an association between depression and sexual risk behaviors [32], more recent studies in PWID and MSM populations have found higher sexual risk associated with depression [34, 35, 40] or a non-linear association [36] in which mild symptoms are most predictive of sexual risk. The few studies that have evaluated the association of depression with injecting risk behaviors among PWID have suggested that depressive symptoms were associated with greater injecting risk behaviors [35, 37–39].

We sought to overcome past methodological issues by using a causal approach to estimate the effect of depressive symptoms on HIV transmission risk behaviors among

PWID. We used marginal structural models, a tool for causal inference that accounts for time-varying exposures and confounders [43–45], with longitudinal data from male PWID living with HIV in Vietnam. We hypothesized that depression would increase behaviors associated with risk of HIV transmission to injecting partners (sharing injection equipment) and sexual partners (condomless sex). By examining depression as a potential underlying cause of HIV transmission through these behavioral mechanisms, we sought to provide clearer evidence about the potential for interventions against depression to avert future HIV infections among PWID.

## Methods

### Parent Trial Design and Population

We used longitudinal data from a randomized controlled trial of an HIV stigma and risk reduction intervention among PWID living with HIV in Thai Nguyen, Vietnam from 2009 through 2013 [46]. Thai Nguyen is a province in northeastern Vietnam with an estimated HIV prevalence of 34% among its approximately 6000 PWID [47–49]. Participants were recruited via snowball sampling from the 32 Thai Nguyen sub-districts (of 180 total) with the most PWID. Recruiters (former and current PWID) approached members of drug networks in private places to discuss study enrollment and then accompanied or referred interested participants to the study site for screening. At screening, all participants were tested for HIV using two rapid enzyme immunoassay tests run simultaneously (Determine: Abbot Laboratories, Abbott Park, IL and Bioline: SD, Toronto Canada), with discordant results resolved with a third rapid assay (HIV Rapid Test: ACON, San Diego, CA). The trial enrolled 455 participants who met the following eligibility criteria: 1) HIV-positive according to study test results, 2) male (given that 97% of PWID in Thai Nguyen are male), 3) age  $\geq 18$  years, 4) had sex in the past 6 months, 5) injected drugs in the previous six months, and 6) planned to live in Thai Nguyen for the next 24 months (the duration of the trial).

### Measures

Questionnaire and laboratory data were collected at study visits every 6 months during 24 months of follow-up. The questionnaire collected information on demographics, injection drug use and other substance use, sexual behavior, depressive symptoms, quality of life, pre-study HIV diagnoses (baseline only), and ART use. Blood specimens were collected to confirm HIV infection at baseline and measure CD4 cell count at baseline and over follow-up.

The exposure of interest was depressive symptoms over the past week, as assessed by the 20-item Center for Epidemiologic Studies Depression Scale (CES-D), which has been validated as a reliable measure of depressive symptoms in Vietnam [50, 51]. Consistent with past work, we defined severe depressive symptoms as CES-D scores  $\geq 23$ , mild depressive symptoms as scores 16–22, and no symptoms as scores  $< 16$  [15, 50–52]. The transmission risk behavior outcomes were any sharing of injection equipment (needles, syringes, solutions, or distilled water) and any condomless sex with a female partner, reported for the prior 3 months. We also descriptively examined the numbers of injection equipment sharing and condomless sex acts in the prior 3 months reported at each visit.

Questionnaire and laboratory data included potential confounders of the depression-risk behavior relationship. Time-fixed covariates, which were reported at baseline and assumed to be stable throughout the study period, were marital status, age, employment status, intervention arm, history of overdose, alcohol use, HIV diagnosis prior to enrollment, and previous ART use. Employment and alcohol use could, in theory, vary over time, but these variables remained fairly constant in our population, motivating our decision to treat them as time-fixed. Time-varying covariates measured at one time point may affect subsequent depression and risk behaviors; they may also be influenced by depression and risk behaviors from a previous time point. Thus, time-varying covariates may act as either confounders or mediators, depending on the time point assessed [41, 43]. For this analysis, time-varying covariates were CD4 cell count category ( $< 200$ , 200–499,  $\geq 500$  cells/ $\mu\text{L}$ ), depressive symptoms at the visit prior to exposure measurement, and transmission risk behaviors at the visit prior to exposure measurement.

## Data Analysis

In the main analysis, we used marginal structural models to estimate the average causal effect of severe depressive symptoms on the risks of any injection equipment sharing or any condomless sex (separately) in the period three to 6 months later, controlling for time-fixed and time-varying confounders. We evaluated each risk behavior outcome (reported with respect to the prior 3-month period) at the next 6-month visit in order to temporally separate it from the exposure of depressive symptoms (hereafter referred to as the “longitudinal effect”). In a second analysis, to facilitate comparison with prior research, we used marginal structural models to estimate the association between depressive symptoms and risk behaviors reported at the same visit, where temporal ordering could not be differentiated (“cross-sectional association”). We repeated both analyses using three levels of depressive symptoms (severe, mild, none) in addition to the binary categorization (severe, not severe).

We used inverse probability weighted estimation of marginal structural models [43, 53]. Weights were estimated from a propensity score model for the probability of severe depressive symptoms as a function of time-fixed and time-varying confounders. Time-fixed confounders had a constant (baseline) value over all visits; time-varying confounders used the value from the visit immediately preceding the visit at which depressive symptoms were assessed. In the main analysis, the propensity score model was estimated using logistic regression to model the probability of severe (vs. mild or no) depressive symptoms. In a second set of analyses, we used ordinal logistic regression to separately model the three levels of depressive symptoms (severe vs. mild vs. none). Propensity score model diagnostics assessed positivity for all confounder-defined subsets of the study population. The denominator of the weights was the predicted probability of depressive symptoms from the propensity score model, and weights were stabilized using the marginal probability of depressive symptoms in the numerator.

Application of the weights to the study population removes the association between depressive symptoms and potential confounding variables included in the propensity score model, permitting estimation of a causal effect under key assumptions [53, 54] (see [Discussion](#)). In the weighted study population, we estimated the risk difference (RD) for the risk behavior outcomes using generalized estimating equations (binomial regression models with an identity link) to account for repeated observations on participants [55–57]. For the longitudinal analysis, this weighted RD can be interpreted as the causal effect of depressive symptoms on the risk behavior outcome: that is, the difference in risk of the behavior in the period three to 6 months later if all participants had depressive symptoms compared with the risk if they all did not have depressive symptoms.

To account for missing data due to missed study visits, we used multiple imputation by chained equations (MICE) [58, 59], imputing and analyzing 50 datasets. We included participants who were incarcerated or died during the study period in the main analysis up until the start of the 6-month follow-up interval during which incarceration or death occurred, censoring them after their final visit preceding death or incarceration. In sensitivity analyses, we instead used the imputed risk behavior outcome for that 6-month interval (and censored them at the start of the following interval), given the possibility of engaging in unmeasured risk behaviors prior to incarceration or death. For all estimates, our interpretation focuses on the point estimate and confidence interval, rather than statistical significance [60]. Analyses were conducted using R Version 3.4.3 [61].

## Ethics

This study was approved by the ethical review committees at all participating institutions. Written informed consent was obtained from all participants.

## Results

As required by inclusion criteria, all 455 participants were male, HIV-positive, and reported being sexually active and using injection drugs at baseline. The median age of participants was 35 years (interquartile range [IQR]: 30, 39), and half were married or cohabitating (47%) (Table 1). One-third had a high school education (34%), and the majority were employed full-time (69%). Most participants were newly HIV-diagnosed at baseline (74%), while 15% had been previously diagnosed and were not taking ART, and 11% reported being previously diagnosed and currently using ART. The median CD4 cell count was 241 cells/ $\mu$ L (IQR: 126, 370). General health was rated as poor by 30%. Nearly half reported injecting heroin daily (45%), 18% had a history of overdose, and 67% reported current alcohol use.

Participants completed between zero and four follow-up study visits (median = 4, IQR: 2, 4) at 6-month intervals over 24 months, with 87% completing at least one follow-up visit.

At baseline, 44% of participants reported severe depressive symptoms ( $CES-D \geq 23$ ), 25% had mild symptoms ( $16 \leq CES-D \leq 22$ ), and 30% had no symptoms ( $CES-D < 16$ ). One quarter of participants reported sex without a condom in the prior 3 months (24%), with a median of 10 condomless sex acts reported for that period (IQR: 5, 20). Most participants reported sharing injection drug use equipment with injecting partners over the past 3 months (73%); these participants reported a median of 21 sharing acts during that period (IQR: 7, 52).

After the baseline visit—when all participants received risk reduction counseling and the majority became newly HIV-diagnosed—sharing injection equipment and condomless sex decreased across trial arms (previously reported in [46]). However, among the 397 participants attending  $\geq 1$  follow-up visit, 21% reported sharing injection equipment at  $\geq 1$  visit, and 7% reported condomless sex at  $\geq 1$  visit. The severity of depressive symptoms varied over time (Supplemental Fig. 1) with 59% of those attending  $\geq 1$  follow-up visit reporting severe depressive

**Table 1** Characteristics of HIV-positive male PWID in Thai Nguyen, Vietnam at baseline and follow-up visits at 6, 12, 18, and 24 months

Characteristic at baseline (n = 455 participants)	Median (IQR) or N (%) <sup>†</sup>
Age in years (range 19–60)	35 (30, 39)
Married or cohabitating	215 (47)
High school education or greater	153 (34)
Full-time employment	315 (69)
Newly diagnosed with HIV	336 (74)
Prior HIV diagnosis, no ART use	68 (15)
Prior HIV diagnosis, current ART use	51 (11)
CD4 cell count (cells/ $\mu$ L)	241 (126, 370)
Self-rated health as poor	136 (30)
Daily injection drug use	207 (45)
History of overdose	84 (18)
Current alcohol use	307 (67)
Severe depressive symptoms ( $CES-D \geq 23$ )	201 (44)
Any sharing of injection equipment in prior 3 months	332 (73)
Number of sharing acts in prior 3 months (if reported any)	21 (7, 52)
Any condomless sex in prior 3 months	108 (24)
Number of condomless acts in prior 3 months (if reported any)	10 (5, 20)
Characteristic over follow-up (n = 397 attended $\geq 1$ visit)	Median (IQR) or N (%) <sup>‡</sup>
CD4 cell count (cells/ $\mu$ L)	251 (148, 376)
Any severe depressive symptoms ( $CES-D \geq 23$ )	235 (59)
Any sharing of injection equipment in prior 3 months	82 (21)
Any condomless sex in prior 3 months	29 (7)

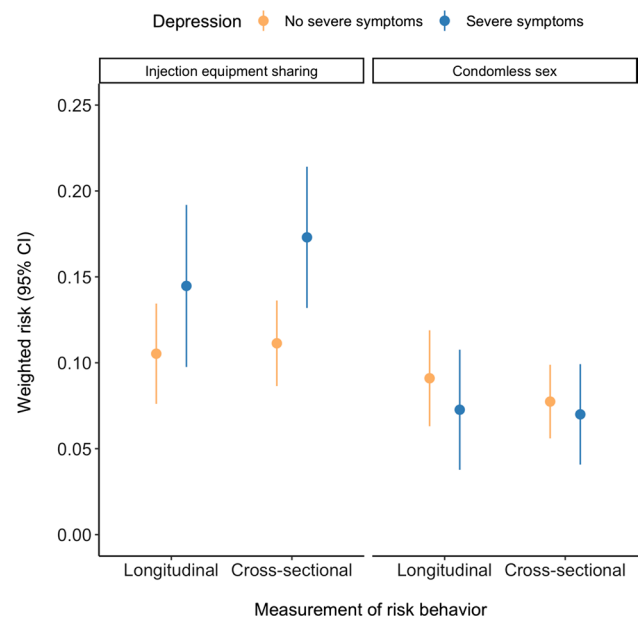
<sup>†</sup>Median and N (%) at baseline visit for all n = 455 participants

<sup>‡</sup>Median and N (%) across all follow-up visits for n = 397 participants who attended at least one follow-up visit

symptoms at least once. The percentage of participants experiencing competing events increased over time, with 8% incarcerated and 23% deceased at 24 months.

In our main analysis, we estimated that severe depressive symptoms (compared to no or mild symptoms) increased the risk of sharing injection equipment by 3.9 percentage points (RD = 3.9%, 95% CI -1.7%, 9.6%) and decreased the risk of condomless sex by 1.8 percentage points (RD = -1.8%, 95% CI -6.4%, 2.8%) in the period three to 6 months later (Table 2, Fig. 1). In the cross-sectional analyses, the association between severe depressive symptoms and contemporaneous injection equipment sharing (RD = 6.2%, 95% CI 1.4%, 11.0%) was stronger than the estimated longitudinal effect, while the association with condomless sex was attenuated (RD = -0.7%, 95% CI -4.5%, 3.0%).

In analyses using three levels of depressive symptoms, there were small decreases in the risk of condomless sex as depressive symptoms increased, although all confidence intervals overlapped substantially (Table 2, Fig. 2). For injection equipment sharing, patterns of risk corresponding to the three levels of depressive symptoms differed between the longitudinal effect and the cross-sectional association. In longitudinal analyses, we observed a U-shaped relationship in which the risk of injection equipment sharing in the period three to 6 months later was 12.8% (95% CI 8.1%, 17.6%) among those with no depressive symptoms, 9.2% (95% CI 5.3%, 13.2%) among those with mild symptoms, and 13.8% (95% CI 9.1%, 18.5%) among those with severe symptoms. In contrast, in the cross-sectional analysis, we observed a monotonic increasing relationship in which those with no



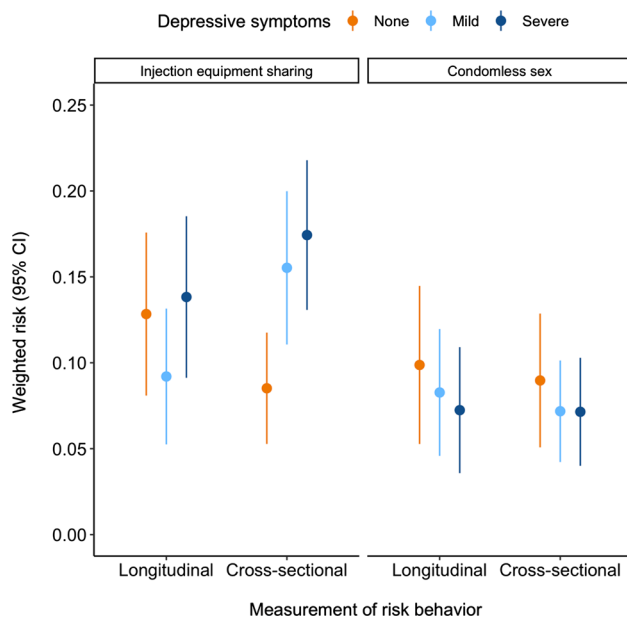
**Fig. 1** Weighted risks of any sharing of injection equipment and any condomless sex by depressive symptoms, estimated among 455 PWID with HIV in Thai Nguyen, Vietnam. Severe depressive symptoms were defined as CES-D ≥ 23; no severe symptoms were CES-D < 23. We evaluated the risk behavior outcome at the next 6-month visit (longitudinal) to estimate the causal effect, and for comparison, we modeled the association at the same visit (cross-sectional)

depressive symptoms had the lowest risk of 8.5% (95% CI 5.3%, 11.8%) while those with mild symptoms had a risk of 15.5% (95% CI 11.1%, 20.0%) and those with severe symptoms had a risk of 17.4% (95% CI 13.1%, 21.8%).

**Table 2** Weighted risk differences (RDs) in percentage points for risk behavior outcomes by depressive symptoms, estimated among 455 PWID with HIV in Thai Nguyen, Vietnam

Injection equipment sharing: main analysis			Injection equipment sharing: three levels of depression		
Depressive symptoms contrast	Risk behavior measurement	RD (95% CI)	Depressive symptoms contrast	Risk behavior measurement	RD (95% CI)
Severe vs. not severe	Longitudinal	3.9 (-1.7, 9.6)	Severe vs. mild	Longitudinal	4.6 (-1.5, 10.7)
Severe vs. not severe	Cross-sectional	6.2 (1.4, 11.0)	Severe vs. none	Longitudinal	1.0 (-6.0, 8.0)
			Severe vs. mild	Cross-sectional	1.9 (-4.4, 8.2)
			Severe vs. none	Cross-sectional	8.9 (3.6, 14.3)
Condomless sex: main analysis			Condomless sex: three levels of depression		
Depressive symptoms contrast	Risk behavior measurement	RD (95% CI)	Depressive symptoms contrast	Risk behavior measurement	RD (95% CI)
Severe vs. not severe	Longitudinal	-1.8 (-6.4, 2.8)	Severe vs. mild	Longitudinal	-1.0 (-6.3, 4.2)
Severe vs. not severe	Cross-sectional	-0.7 (-4.5, 3.0)	Severe vs. none	Longitudinal	-2.6 (-8.7, 3.5)
			Severe vs. mild	Cross-sectional	-0.0 (-4.5, 4.4)
			Severe vs. none	Cross-sectional	-1.8 (-6.8, 3.2)





**Fig. 2** Weighted risks of any sharing of injection equipment and any condomless sex exploring three levels of depressive symptoms. The three levels of symptoms were severe ( $CES-D \geq 23$ ), mild ( $16 \leq CES-D < 22$ ), and none ( $CES-D < 16$ ). For each comparison, we evaluated the risk behavior outcome at the next 6-month visit (longitudinal) to estimate the causal effect as well as the association at the same visit (cross-sectional)

We did not find appreciable differences in sensitivity analyses that varied censoring time for participants who were incarcerated or deceased (Supplemental Fig. 2).

## Discussion

Using longitudinal data and methods for causal inference, we found that severe depressive symptoms increased the risk of sharing injection equipment but not the risk of condomless sex among PWID. To overcome past methodological issues, we used marginal structural models to capture the episodic nature of depression, enforce temporal ordering of depression and transmission risk behaviors, and control time-varying confounding in the analysis. By focusing on PWID living with HIV in Vietnam, a population at high risk of ongoing HIV transmission, we aimed to better understand depression as an underlying cause of behaviors associated with transmission.

In our main analysis of injection equipment sharing in the period three to 6 months after assessment of depression, we found a RD of 3.9% (95% CI  $-1.7\%$ ,  $9.6\%$ ), comparing participants with severe depressive symptoms to those with mild or no depressive symptoms. This longitudinal effect was only slightly weaker than the corresponding cross-sectional association (RD = 6.2%, 95% CI 1.4%,

11.0%) found in the analysis that did not enforce temporality. The 95% CI of the longitudinal effect ( $-1.7\%$ ,  $9.6\%$ ) shows that a risk difference ranging from a 1.7 percentage point decrease, a small negative association, to a 9.6 percentage point increase, a substantial positive association, is compatible with the data. Given that the overall risk of injection equipment sharing was 10% across follow-up visits, the point estimate of a 3.9% point increase is substantively meaningful.

Previous research has suggested a possible non-linear relationship between the severity of depressive symptoms and occurrence of sexual risk behaviors, although this literature has focused on MSM, not PWID, and findings have been mixed. Some studies have found that mild depressive symptoms are associated with higher levels of sexual risk behavior but decreasing risk with severe depressive symptoms [25, 36]; others have observed increasing risk with increasing severity of depressive symptoms [26–28]. In contrast, our analysis of condomless sex according to three levels of depressive symptoms suggested slight decreases in condomless sex with increasing severity of depressive symptoms, consistent with our main analysis. Participants with depressive symptoms – regardless of severity – may be experiencing fatigue, social isolation, and loss of interest in sex, thereby reducing the risk of engaging in this behavior [62]. Although all participants reported sex in the 6 months prior to baseline (due to trial eligibility criteria), a loss of interest in sex over 24 months of follow-up, particularly among participants with depressive symptoms, may have contributed to our findings.

In contrast to condomless sex, we observed possible non-linearities in the relationship between depressive symptom severity and risk of sharing injection equipment, which have not been observed previously. Prior studies have found an increasing risk of injecting risk behavior with increasing depressive symptom severity [38] or have not differentiated between mild and severe symptoms [35, 37, 39]. We found monotonically increasing risk with increasing depressive symptoms in our cross-sectional analysis, and a U-shaped risk in our longitudinal analysis, where those with mild depressive symptoms had the lowest risk. Interestingly, the U-shaped relationship we observed for longitudinal injecting risk is the inverse of some previous findings on sexual risk among MSM (where those with mild depressive symptoms had the highest risk) [36]. This may be due to mild depressive symptoms manifesting differently for injecting behavior compared to sexual behavior and inherent differences between PWID and MSM populations. Depressive symptoms could lead to cognitive distortions, maladaptive coping, and loss of risk aversion [63–65], and such symptoms may need to become severe in order to be expressed behaviorally as increased frequency of injection drug use (to treat severe symptoms) and consequently, greater sharing of equipment.

Although various relationships between depression and HIV transmission risk behaviors have been studied previously, the unique contributions of this study are its focus on PWID living with HIV, a population for whom there is limited data on depression and risk behaviors, and its methodological rigor in inferring causality rather than correlation. Our modeling approach controlled time-varying confounding and incorporated the episodic nature of depressive symptoms by using longitudinal data from five study visits over 2 years. Given that the longitudinal effect enforced temporal ordering of depressive symptoms prior to risk behaviors, we believe that it more closely reflects the causal effect than does the cross-sectional association. However, it is important to consider the trade-off between temporal ordering and etiologic relevance in the context of data limitations particular to this study. Separating the measurement of depressive symptoms and risk behaviors by 6 months (with a 3-month “blackout period” in between) was necessitated by the parent trial’s data structure. This incomplete interval coverage could have attenuated effect estimates relative to what they might have been if the entire interval were included (that is, if depressive symptoms were more likely to influence risk behaviors in the first 3 months of the follow-up interval). A shorter time interval with more complete data coverage may allow better capture of the effect of episodic depressive symptoms on subsequent risk behavior.

Inferring causality relies on several key assumptions, which must be evaluated carefully in light of the limitations of this observational study [53, 54]. The assumption of no unmeasured confounding holds that there are no systematic differences between participants with and without depression beyond any differences in variables controlled for in the analysis. Although we controlled for a variety of confounders, it is possible that unmeasured confounding biased estimates of the effect of depression on risk behaviors. We also assumed positivity (i.e., participants with and without depressive symptoms were in all confounder-defined subsets of the population) and that models were correctly specified without measurement error for covariates. Importantly, this study’s ascertainment of depression relied on CES-D score categories, and the CES-D is not diagnostic of clinical depression. However, we used a conservative cut-point for severe depressive symptoms with high reliability and validity [50, 51]. There may also have been under-ascertainment of risk behaviors due to social desirability and recall bias. However, participants reported high levels of drug use and had been recruited by former drug users (aware of their injection drug use), indicating a willingness to disclose sensitive behaviors. Finally, the consistency assumption holds that there is no meaningful variability in treatment relevant to its effect on the outcome. Here, we did not model a specific treatment on depression, and results should only be interpreted as the hypothetical effect of eliminating severe

depressive symptoms without specifying the treatment used for elimination.

Our conclusions are specific to this study population, which was not randomly sampled and may not be representative of all PWID living with HIV. While men who inject drugs drive the HIV epidemic in Vietnam, our findings may not be applicable to other groups, such as women or PWID in other regions. However, our findings may be broadly generalizable to other Asian and European countries where the HIV epidemic is concentrated among similar groups. We also note that the sample size of this hard-to-reach population was relatively small, which limited our statistical power to detect small differences in risk between depression groups. Importantly, the risk behavior outcome in our study does not allow direct prediction of forward HIV transmission risk, as we did not take into account viral suppression status, the frequency of risk acts, or partner susceptibility to HIV. These determinants of transmission will be incorporated into a future mathematical modeling analysis that will explicitly estimate forward transmission events from this study population.

We found that severe depressive symptoms may perpetuate the risk of sharing injection equipment among PWID living with HIV in Vietnam. During the study period (2009–2013), there was very limited access to mental health services for people living with depression in Vietnam [66]. However, in recent years, mental health services have become a national health priority, and there is growing attention and funding for increasing local services and availability of depression treatment [66, 67]. Screening and treating depressive symptoms among PWID presents an opportunity not only to improve mental health and drug abuse outcomes but also to reduce behaviors associated with HIV transmission risk.

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## Compliance with Ethical Standards

**Conflicts of interest** None.

**Ethical Approval** This research was approved by the ethical review committees at the Thai Nguyen Center for Preventive Medicine, the

Johns Hopkins Bloomberg School of Public Health, and the University of North Carolina at Chapel Hill Gillings School of Global Public Health. All procedures performed were in accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

**Informed Consent** Written informed consent was obtained from all participants.

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